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Parp Inhibitor in advanced Non-small cell lung cancer

Submission date	Recruitment status	[X] Prospectively registered
08/11/2013	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/11/2013	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
26/05/2021	Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-looking-olaparib-non-small-cell-lung-cancer-pin

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01788332

Clinical Trials Information System (CTIS)
2012-003383-51

Protocol serial number
15521

Study information

Scientific Title
A randomised phase II trial of Olaparib maintenance versus placebo monotherapy in patients with chemosensitive advanced non-small cell lung cancer

Acronym
PIN

Study objectives
The purpose of this trial is to find out whether giving a drug called olaparib following chemotherapy will benefit patients with NSCLC who have responded to initial chemotherapy treatment by prolonging the time before the tumour re-grows. 114 patients who have responded to chemotherapy will be randomly allocated to receive either olaparib or placebo tablet by mouth. The rationale for this clinical trial is that chemotherapy damages tumour cell DNA and that NSCLC tumours that respond to chemotherapy are less able to repair this damage. This can be exploited by using olaparib, a drug which blocks an enzyme called PARP which is essential for DNA repair. This will prevent DNA repair and cause cancer cell death by a mechanism known as synthetic lethality. Synthetic lethality arises when a combination of mutations in two or more genes leads to cell death. If this study shows that olaparib does delay disease progression, a larger more detailed clinical trial will be needed to find out whether using olaparib actually makes patients live longer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
13/WA/0117; First MREC approval date 07/06/2013

Study design
Multicentre double blind randomised phase II trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Lung Cancer; Disease: Lung (non-small cell)

Interventions
Patients are initially registered before induction chemotherapy, their response to which will be used to determine whether they are eligible for randomisation. All patients will be asked to consent to archival tissue collection for translational analysis and to provide a translational blood sample. The second consent will precede randomisation to one of two groups of maintenance therapy (Olaparib or placebo) with 1:1 randomisation if they have had an objectively measured complete or partial response following standard chemotherapy. Randomised patients will receive Olaparib (300mg, two 150mg tablets, to be taken twice a day) or placebo until disease progression. They will be monitored by CT scan every two cycles until

disease progression, when they will be managed according to local practice. Follow up will be for a maximum of 12 months from the point of randomisation or until disease progression.

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
Progression free survival (PFS); Timepoint(s): Will be analysed after 98 PFS events

Key secondary outcome(s))
1. Change in tumour volume reduction; Timepoint(s): From randomisation to 6 weeks
2. Objective response rate; Timepoint(s): As assessed by Response Evaluation Criteria In Solid Tumors (RECIST) v1.1
3. Overall survival; Timepoint(s): Time from randomisation to death with those still alive censored at date last seen
4. Safety, tolerability and feasibility of use; Timepoint(s): Will be assessed in real time

Completion date
01/12/2014

Eligibility

Key inclusion criteria
At registration:
1. Histological diagnosis of NSCLC. Histology can be either squamous or nonsquamous. The same block or 10 unstained slides must be available for translational research.
2. Stage IIIB or stage IV lung cancer, that is not amenable to curative therapy
3. Eastern Cooperative Oncology Group (ECOG) performance status 01
4. Have had no prior systemic treatment for lung cancer including previous adjuvant and neoadjuvant therapy. Patients who have already started their induction chemotherapy are not eligible.
5. Eligible to receive standard platinum doublet-based chemotherapy
6. Men or women, aged 18 or over and capable of giving informed consent
7. Willing to consent to provide tissue and blood for translational research
8. Informed consent prior to any study procedures.

At randomisation:
1. Partial or complete response to platinum containing doublet chemotherapy after a minimum of 3 cycles, as assessed by the local radiologist
2. Adequate organ function, including the following:
2.1. Adequate bone marrow reserve: absolute neutrophil count (ANC) = 1.5 x 10^9/L, platelets = 100 x 10^9/L , Haemoglobin of = 10g/dL
2.2. Hepatic: total bilirubin = 1.5 times the upper limit of normal (x ULN); alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) = 2.5 x ULN. ALP, AST, and ALT = 5 x times ULN is acceptable if the liver has tumour involvement
2.3. Renal: calculated creatinine clearance (CrCl) = 50mL/min based on the original weight based Crockcroft and Gault formula, Serum creatinine = 1.5 x institutional upper limit of normal (ULN)
2.4. If blood count suggestive of MDS/AML, no features suggestive of MDS/AML on peripheral

blood smear
3. Patients with reproductive potential must be prepared to use adequate contraception throughout the study and for three months after the last dose of Olaparib
4. Informed consent prior to any study specific procedures
Target Gender: Male & Female

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
70

Key exclusion criteria
At registration:
1. Evidence of small cell, large cell neuroendocrine or carcinoid histology
2. Have a serious or uncontrolled medical condition that in the opinion of the investigator would compromise the patients ability to adhere to the protocol
3. Have a secondary malignancy (except adequately treated non-melanomatous skin cancer, or other cancer that is considered cured by surgical resection or radiation). Patients who had another malignancy in the past but have been disease free for more than 5 years, are eligible.
4. Have had a blood transfusion within 4 weeks prior to entry and have a WBC >3 x 10^9/L
5. Have central nervous system (CNS) metastases (unless the patient has completed successful local therapy for CNS metastases eg. Involving complete surgical removal or radical radiotherapy to a solitary CNS metastasis)
6. Are receiving concurrent administration of any other systemic antitumour therapy
7. Have received a recent (within 30 days of enrolment) or are receiving a concurrent yellow fever vaccination
8. Previous treatment with PARP inhibitors
9. Difficulty swallowing
10. Uncontrolled GI disorders such as active diverticulitis or colitis, or any major GI resection which could have an impact on patients' ability to absorb Olaparib
11. Patients with myelodysplastic syndrome/Acute myeloid leukaemia
12. Congenital long QT syndrome

At randomisation:
1. Patients with radiological disease progression or stable disease
2. Have received treatment with an agent that has not received regulatory approval, within 30 days of study entry
3. Have had a blood transfusion within 4 weeks prior to entry and have a WBC >3 x 10^9/L

4. Resting ECG with QTc>/480 msec
5. Are pregnant or breastfeeding

Date of first enrolment
01/12/2013

Date of final enrolment
01/12/2014

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
6th Floor, Neuadd Meirionnydd
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Sponsor information

Organisation
Velindre NHS Trust (UK)

ROR
https://ror.org/05ntqkc30

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca Limited (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			28/05/2020	No	No
HRA research summary			28/06/2023	No	No
Plain English results				No	Yes